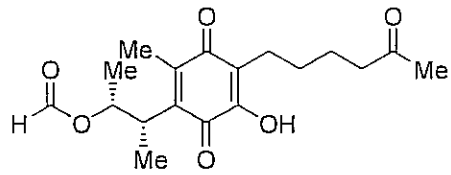
ABSTRACT

Unequivocally fungi are the best source in providing lead compounds for discovery and development of therapeutic agents. In the past, fungi have performed impressive roles in development of drugs and recent findings have shown that they are promising in fulfilling future needs especially in treatment of cancer.

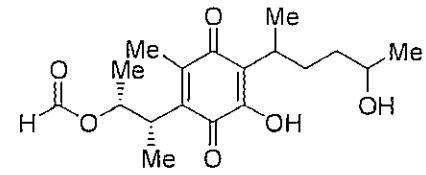
The thesis consists of three chapters. Natural product-derived drug leads isolated from microorganisms with special reference to fungi, and metabolites isolated from *Penicillium citrinum* and *Aspergillus terreus*, covering literature published up to 2012 is reviewed in the chapter 1. Chapter 2 describes the bioactivity directed chemical investigation of ethyl acetate (EtOAc) extracts of two terrestrial fungal isolates, *P. citrinum* and *A. terreus*. The third chapter describes all experimental procedures followed.

A preliminary investigation carried out on two fungal cultures, *P. citrinum* and *A. terreus* revealed that EtOAc extracts of both cultures showing antibacterial activity against *Bacillus* sp. and *Staphylococcus* sp. Therefore, further studies on these two fungi were undertaken. Bioactivity guided fractionation of EtOAc extracts of each culture grown in Potato dextrose agar was carried out using solvent-solvent partitioning, column chromatography followed by preparative thin layer chromatography to isolate the bioactive constituents.

Fractionation of EtOAc extract of *P. citrinum* afforded two hitherto unknown 1, 4- benzoquinones, citriquinone A and B. Structures of these two new metabolites were elucidated using detailed spectroscopic analysis.



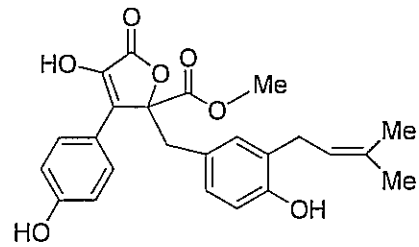
Citriquinone A



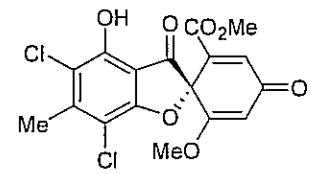
Citriquinone B

Antibacterial assay carried out on Citriquinone A revealed that it is moderately active against *Bacillus sp.* giving an average clear zone (CZ) of 16 mm at a dose of 250 μg/ disc while 25 μg of amoxicillin (positive control) gave a CZ of 12 mm. When subjected to cell migration inhibition assay (CMIA) on human cancer cell line HEp 2 maintained *in-vitro*, Citriquinone A inhibited growth/migration of cells when compared to the control (1% dimethyl sulfoxide) at a concentration of 0.5 mg/ mL indicating its potential anticancer activity.

Bioactivity directed fractionation of EtOAc extract of *A. terreus* afforded two known fungal metabolites butyrolactone I and (+)-geodin. Their structures were elucidated by detailed spectroscopic analysis and confirmed by the comparison of spectroscopic data with those reported.



Butyrolactone I



(+)-Geodin

Both compounds found to be active against *Bacillus* sp. tested. Activity of butyrolactone I (150 μg/disc) was equivalent to the activity of 25 μg of Amoxicillin (CZ for each = 14.0 mm), while 25 μg of (+)-geodin showed a higher activity (CZ = 14.5 mm) than an equivalent dose of Amoxicillin (CZ = 12.5 mm).